Epigenetic stability, adaptability, and reversibility in human embryonic stem cells.

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Public Summary:

Scientific Abstract:
The stability of human embryonic stem cells (hESCs) is of critical importance for both experimental and clinical applications. We find that as an initial response to altered culture conditions, hESCs change their transcription profile for hundreds of genes and their DNA methylation profiles for several genes outside the core pluripotency network. After adaption to conditions of feeder-free defined and/or xeno-free culture systems, expression and DNA methylation profiles are quite stable for additional passaging. However, upon reversion to the original feeder-based culture conditions, numerous transcription changes are not reversible. Similarly, although the majority of DNA methylation changes are reversible, highlighting the plasticity of DNA methylation, a few are persistent. Collectively, this indicates these cells harbor a memory of culture history. For culture-induced DNA methylation changes, we also note an intriguing correlation: hypomethylation of regions 500-2440 bp upstream of promoters correlates with decreased expression, opposite to that commonly seen at promoter-proximal regions. Lastly, changes in regulation of G-coupled protein receptor pathways provide a partial explanation for many of the unique transcriptional changes observed during hESC adaptation and reverse adaptation.

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